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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/337,675	06/22/1999	RAJEEV A. JAIN	029318/0497	9275

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EXAMINER
PULLIAM, AMY E

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 07/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/337,675	Applicant(s) JAIN ET AL.	
	Examin r Amy E Pulliam	Art Unit 1615	

-- Th MAILING DATE of this communication app ars on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/17/02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22 and 25-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 25-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *19,23* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of the Request for an RCE, the Information Disclosure Statement, the Request for Reconsideration and RCE resubmission, and the Supplemental Amendment C, received by the Office October 10, 2001, January 3, 2002, December 3, 2001, and May 17, 2002, respectively.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 sand 31 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the

present instance, claims 2 and 31 recite the broad recitation, "consisting of less than about 800 nm," and the claims also recite, "less than about 600 nm, less than about 400 nm, less than about 300 nm, less than about 250 nm, less than about 100 nm, and less than about 50 nm," which is the narrower statement of the range/limitation. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-22, and 25-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,145,684 to Liversidge *et al.* (hereinafter Liversidge). Liversidge discloses dispersable particles made of a drug substance and a surface modifer adsorbed on the surface of the drug, to maintain an effective average particle size of less than about 400 nm, as well as the method of making the particles through wet grinding. Further, Liversidge teaches that of pharmaceutical formulations containing the nanoparticles, and their use in method of treating mammals (abstract). Liversidge further discloses the drug substance useful in this invention is a poorly soluble drug, chosen from the list in column 3, lines 53+. In addition, Liversidge teaches that the surface modifier of the invention can be selected from various polymers, oligomers, natural products and surfactants. Examples of excipients include gelatin, casein, lecithin, gum acacia and others, and examples of polymers include carboxymethyl cellulose, hydroxyethyl cellulose,

hydroxypropyl cellulose and others (c 4, l 34-55). Liversidge also teaches that pharmaceutical compositions according to this invention include the nanoparticles and a pharmaceutically acceptable carrier, which is well known in the art for making solid or liquid oral formulation (c 7, l 53-60).

]Liversidge does not teach the specific amounts of excipients present in the composition, however, it is the position of the examiner that based on the general teaching of the presence of excipients, and the teaching that Liversidge's composition can be formulated into well known forms, including solid oral forms, it is the position of the examiner that the specific concentrations is a specific limitations which would be routinely determined by one of ordinary skill in the art through minimal experimentation, as being suitable, absent the presentation of some unusual and/ or unexpected results. The results must be those that accrue from the specific limitations.

Further, it is the position of the examiner that the teaching of cellulose polymers in the composition reads on applicant's claim to both a surface stabilizer and a rate controlling polymer, because on page 12, lines 27-28, applicant states that a suitable surface stabilizer includes various polymers, therefore the cellulose polymers can perform both desired functions. One of ordinary skill in the art would have been motivated to produce a well known pharmaceutical dosage form, such as a tablet, which incorporates Liversidge's nanoparticles, and the necessary excipients, especially based on Liversidge's disclosure that his particles are intended for this exact purpose. One of ordinary skill in the art would expect a successful pharmaceutical dosage form.

Additionally, applicant has added several new claims drawn to specific surface modifiers and drugs. Liversidge teaches the surface modifiers at column 4, lines 34-55.

Furthermore, Liversidge teaches the broad categories of drugs at column 3, lines 53-68. Liversidge does not teach the specific drugs claimed by applicant. However, it is the position of the examiner that because the reference teaches the same broad drug categories claimed by applicant, one of ordinary skill in the art would have been motivated to use any well known drug which falls within one of those broadly taught categories, because there has been no evidence provided that some drugs behave better than others. The expected result would be a successful pharmaceutical formulation.

Therefore, this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant argues that Liversidge does not teach nanoparticles in a controlled release formulation. Applicant further argues that Liversidge teaches that the rate of dissolution increases with increased surface area (or decrease particle size). Additionally, applicant argues that Liversidge does not teach a surface modifier used to prepare a controlled release dosage form. Lastly, applicant argues that the instant claims require an active agent, a surface modifier, and a rate controlling polymer, while the Liversidge reference only has two of these components.

The examiner respectfully disagrees with applicant's arguments for the following reasons. First, the examiner points out that the disclosure regarding increased dissolution and decrease particle size was made in the background section of the Liversidge reference, and not as part of the actual inventive concept, and therefore does not relate to Liversidge's invention.

Second, there has been no evidence provided to prove that the formulation of Liversidge is not a controlled release formulation, but rather is a rapid release formulation. This is particularly important because the composition of Liversidge contains the same components being claimed by applicant. The examiner requests that applicant provide comparative data, comparing the formulation of Liversidge to applicant's claimed formulation, in order to prove that the two formulations behave differently. The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. *See Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Third, applicant's instant claim 1 requires a controlled release nanoparticulate composition comprising a poorly soluble drug, at least one surface stabilizer, and at least one pharmaceutically acceptable rate controlling polymer. There is nothing in this claim language which prohibits a rate controlling polymer which acts as a surface modifier. And in fact, this is exactly what the Liverside reference teaches. Liversidge discloses a list of suitable surface modifiers and excipients, (listing most of applicant's specific examples) which includes well known rate controlling polymers. It remains the position of the examiner that the rate controlling polymers listed in the reference serve as both

surfactants, and their well known purpose, which is to control release rates. Absent any evidence to the contrary, this remains the examiner's position.

The examiner strongly urges applicant to provide comparative data, further exemplifying any differences between the teachings of Liversidge and the formulation instantly claimed by applicant. This evidence must remain commensurate with the scope of the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E Pulliam whose telephone number is 703-308-4710. The examiner can normally be reached on Mon-Thurs 7:30-5:00, Alternate Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

aep
July 19, 2002

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600